explanation of the relevance of EP 0 088 046 and EP 0 133 988 (references BF and BG in the originally filed PTO-1449), as it is presently understood by the individual designated in 37 C.F.R. § 1.56(c) most knowledgeable about the content of each patent. In addition, the substitute PTO-1449 has been amended to remove reference to EP 0 143 949 (reference BH in the originally filed PTO-1449), since this reference was cited twice (see reference BC). Finally, the substitute PTO-1449 was amended to remove reference to Current Protocols In Molecular Biology (Ausubel et al., eds., John Wiley & Sons 1994); Remington's Pharmaceutical Sciences (Gennaro, ed., Mack Publishing 18th ed. 1990); Computer Analysis of Sequence Data, Part 1 (Griffin et al., eds., Humana Press 1994); Sequence Analysis Primer (Gribskov et al., eds., Oxford University Press 1991); von Heinje, Sequence Analysis in Molecular Biology (Academic Press 1987); Computational Molecular Biology (Lesk, ed., Oxford University Press 1998); Sambrook, Molecular Cloning: A Laboratory Manual (Cold Springs Harbor University Press 1989), Biocomputing: Informatics and Genome Projects (Smith, ed., Academic Press 1993); and Steward et al., Solid Phase Peptide Synthesis (W.H. Freeman & Co. 1984) (references CC, DL, DM, DO, DP, EA, EL, EN, and EO, respectively, in the originally filed PTO-1449). As these references merely reflect the general state of the art at the time the invention was made, Applicants are unable to specifically indicate or provide copies of the relevant pages.

2. Objection to claims 1-8, 10, 11, 46-48, and 55

The Office Action contains an objection to claims 1-8, 10, 11, 46-48, and 55 as being improperly dependent because the claims are dependent upon a non-elected invention. Applicants have amended claims 1-3 to recite only the elected invention.

3. Objection to specification

The Office Action contains an objection to the specification for containing a space on page 106 between the terms "intracerebral" and "(intra-parenchymal)." Applicants note that there is only a single space between these terms, and that the seemingly irregular spacing is due to the length of the term (*i.e.*, "intracerebroventricular") that immediately follows the term "(intra-parenchymal)."

4. Rejections of claims 1-8, 10, 11, 46-48, and 55 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, 46-48, and 55 under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims. The Examiner takes the position that the as-filed specification contemplates several methods of gene therapy using the polynucleotides of the claimed invention, and that it would require undue experimentation to determine how to use these polynucleotides in any method of gene therapy.

First, Applicants disagree with the Examiner's assertion that "the elected invention lies in the field of gene therapy" (p. 4 of Office Action). Applicants contend that the pending claims are directed instead to B7-like nucleic acid molecules. Applicants further contend that the B7-like nucleic acid molecules of the claimed invention are enabled for use in, for example, drug candidate screening assays. Specifically, the instant specification provides the nucleotide sequences of a number of B7-like nucleic acid molecules (e.g., SEQ ID NO: 2, SEQ ID NO: 4, and SEQ ID NO: 6), methods for making a transgenic mouse using the claimed B7-like nucleic acid molecules (section entitled "Genetically Engineered Non-Human Animals" beginning at page 74), and guidance for using the transgenic animals of the present invention to screen for drug candidates (p. 75, ln. 7-28). In view of this disclosure, Applicants contend that the instant specification is enabling for use of the invention commensurate in scope with the claims (i.e., B7-like nucleic acid molecules).

In order to provide a reply to the instant Office Action that is fully responsive, Applicants now turn to the particular rejections asserted in the Office Action. The Examiner first asserts that the specification does not enable claims directed to a method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of any of Claims 1, 2, or 3, because the claimed invention does not specify the polypeptide in the animal to be modulated. Applicants have amended Claim 55 to indicate that the polypeptide to be modulated is a "B7-like polypeptide." The specification defines the term B7-like polypeptide at page 16, line 23 to page 17, line 3. Applicants respectfully contend that this ground of rejection has been overcome by amendment.

The Examiner next asserts that the specification does not enable claims to a pharmaceutical

composition comprising a nucleic acid molecule of Claims 1, 2, or 3. In order to expedite prosecution of the instant application, Applicants have canceled claims 46 and 47 without prejudice or disclaimer, rendering this ground of rejection moot. This amendment has been made solely to expedite prosecution and was not made to overcome prior art.

The Examiner also takes the position that it would require undue experimentation to determine the genetic sequences embraced by the claims of the instant application. The Examiner first asserts that it would not be apparent to one of ordinary skill in the art that nucleic acid molecules encoding a polypeptide having a substitution and/or deletion of 1 to 100 amino acid residues in the polypeptide set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 would have B7-like polypeptide activity. Applicants have deleted Claim 2(g) of the as-filed specification, rendering this ground of rejection moot. The Examiner next asserts that it would not be apparent to one of ordinary skill in the art how nucleotide sequences complementary to the nucleotide sequences of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5 would exhibit B7-like polypeptide activity. Applicants contend that Claims 1(e), 2(k), and 3(l) of the as-filed specification are directed to nucleotide sequences that hybridize to nucleotide sequences that are complementary to the nucleotide sequences of the present invention, and are *not themselves* complementary to the nucleotide sequences of the present invention. Applicants therefore assert that it would be apparent to one with skill in the art how the nucleotide sequences of Claims 1(e), 2(k), and 3(l) would exhibit B7-like polypeptide activity, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment, traversed by argument, or mooted by cancellation of the rejected claims, and request that the Examiner withdraw all rejections made on this basis.

5. Rejections of claims 1-3, 8, 10, and 47 under 35 U.S.C. § 112, second paragraph

The Office Action asserts a rejection of claims 1-3, 8, 10, and 47 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner takes the position that claims 1-3 are indefinite because the phrase "moderately or highly stringent conditions" is not defined by the claims and the specification does not provide a standard for ascertaining the

parameters of such conditions. Applicants note that definitions of "moderately stringent conditions" and "highly stringent conditions" are provided in the specification at page 29, lines 4-13 and page 27, lines 13-24, respectively. As an Applicant is entitled to be his or her own lexicographer, these definitions control the interpretation of the phrase "moderately or highly stringent conditions" as it is used in the claims of the instant application, provided that these definitions are not contrary to the meanings of these terms in the art. Moreover, Applicants contend that it would be apparent to one of ordinary skill in the art, in view of the teachings in the instant specification, whether a particular set of hybridization conditions was either "moderately stringent" or "highly stringent." Therefore, Applicants contend that the claims are not indefinite for reciting the phrase "moderately stringent conditions," and respectfully request withdrawal of this ground of rejection.

The Examiner also takes the position that claims 8 and 10 are indefinite because the phrase "B7-like polypeptide" is not defined by the claims and the specification does not provide a standard for ascertaining the meaning of this phrase. Applicants note that an explicit definition of "B7-like polypeptide" is provided in the specification at page 16, line 23 to page 17, line 3, and contend that this definition controls the interpretation of the phrase "B7-like polypeptide" as it is used in the claims of the instant application. Applicants contend, for example, that it would be apparent to one of ordinary skill in the art that a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 is a B7-like polypeptide. Applicants further contend that it would be apparent to one of ordinary skill in the art that a polypeptide variant (e.g., a polypeptide having at least one conservative amino acid substitution) of the amino acid sequence of SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6 is a B7-like polypeptide, provided that the polypeptide variant has an activity of the polypeptide as set forth in SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6. Therefore, Applicants contend that the claims are not indefinite for reciting the phrase "B7-like polypeptide," and respectfully request withdrawal of this ground of rejection.

The Examiner further takes the position that claim 47 is indefinite because the limitation "[a] composition of claim 46" lacks an antecedent basis. Applicants have canceled claim 47, rendering this ground of rejection moot.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been traversed by argument or mooted by cancellation of the rejected claims, and request that

the Examiner withdraw all rejections made on this basis.

8. Rejections of claims 1-3 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1-3 under 35 U.S.C. § 102, as being anticipated by Marra *et al.* (The Washington University-NCI Mouse EST project, seq_name: gb_est82:BF040046, July 2, 1999; GenBank Accession No. AI790785), contending that Marra *et al.* disclose an EST sequence that shares 85% similarity with the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5, and therefore would hybridize under moderately stringent conditions to nucleic acid molecules comprising these nucleotide sequences. Applicants traverse this rejection.

Marra et al. disclose a nucleotide sequence of 530 bp. SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5 set forth nucleotide sequences of 1146 bp, 1158 bp, and 1158 bp, respectively. Exhibits A-C indicate that there is an overlap of no more than 274 bp or 286 bp between the nucleotide sequence disclosed by Marra et al. and the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5. Exhibits A-C also indicate that in the overlapping regions, the sequences share an identity of between 69.6% to 72.6%, and not 85% (Applicants understand the Office Action to mean 85% identity, rather than similarity, since the term "similarity" refers to the degree of sequence relatedness between two polypeptide sequences, and is defined as such in the instant specification at page 21, lines 6-20). Applicants contend that because the nucleotide sequence of Marra et al. and the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 5 share no more than 72.6% identity over no more than 286 bp, a nucleic acid molecule comprising the nucleotide sequence of Marra et al. would not hybridize under moderately stringent conditions to nucleic acid molecules comprising the nucleotide sequences set forth in SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5. Therefore, Applicants contend that Marra et al. does not anticipate claims 1-3, and respectfully request that the Examiner withdraw this rejection.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.



Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

- 1. (Amended) An isolated nucleic acid molecule comprising-a nucleotide sequence selected from:
- (a) the nucleotide sequence as set forth in <u>any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5-or 7</u>;
 - (b) the nucleotide sequence as set forth in SEQ ID NOs: 9, 11 or 13;
- (c)(b) a nucleotide sequence encoding the polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8;
- (d) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- (e)(c) a nucleotide sequence which hybridizes under at least moderately-or highly stringent conditions to the complement of the nucleotide sequence of either (a) or (b), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8; or
- (f) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of (a) or (b), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14; and
 - (g)(d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) (f)(c).
- 2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from:
- (a) a nucleotide sequence encoding a polypeptide that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98 or 99 percent identical to the polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8, wherein the encoded polypeptide has an activity of the mature form of a-polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8;

 (b) a nucleotide sequence encoding a polypeptide that is at least about 70, 75, 80, 85, 90,
- 95, 96, 97, 98 or 99 percent identical to the polypeptide as set forth in SEQ ID NOs: 10, 12 or 14,

wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;

- (c)(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5-or-7, or the nucleotide sequence of (a), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8;
- (e)(c) a region of the nucleotide sequence of any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5-or-7, or the nucleotide sequence of (a) or (b), above, encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide fragment has an activity of the mature form of a encoded polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8, or is antigenic;
- (f) a nucleotide sequence of SEQ ID NOs: 9, 11 or 13, or (a) or (b), above, encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- g) a nucleotide sequence encoding a polypeptide that has a substitution and/or deletion of 1 to 100 amino acid residues as set forth in any of SEQ ID NOs: 1, 3, 5 or 7, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 2, 4, 6 or 8;
- h) a nucleotide sequence encoding a polypeptide that has a substitution and/or deletion of 1 to 100 amino acid residues as set forth in any of SEQ ID NOs: 9, 11 or 13, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- (i)(d) a region of the nucleotide sequence of any of SEQ ID NOs: 1, SEQ ID NO: 3, or SEQ ID NO: 5 or 7, or the nucleotide sequence of any of (a), -(c), (e) or (g), above, comprising a fragment of at least about 16 nucleotides;
- (j) a nucleotide sequence of SEQ ID NOs: 9, 11 or 13, or (b), (d), (f) or (h), above,

comprising a fragment of at least about 16 nucleotides;

- (k)(e) a nucleotide sequence which hybridizes under at least moderately or highly stringent conditions to the complement of the nucleotide sequence of any of (a), (c), (e), (g) or (i) (d), above, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8; or
- (1) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (b), (d), (f), (h) or (j), above, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14; and
 - (m)(f) a nucleotide sequence complementary to the nucleotide sequence of any of (a) (1)(e).
- 3. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from:
- (a) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8;
- (b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- (e)(b) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8;
- (d) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 with at least one amino acid insertion, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- (e)(c) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2,

SEQ ID NO: 4, or SEQ ID NO: 6-or 8;

- (f) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 with at least one amino acid deletion, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- (g)(d) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8 which has a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8;
- (h) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 which has a C- and/or N- terminal truncation, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- (i)(e) a nucleotide sequence encoding a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8 with at least one modification that is a-selected from at least one conservative amino acid substitution, an amino acid insertion, an amino acid deletion, C-terminal truncation, andor N-terminal truncation, wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or 8;
- (j) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14 with at least one modification selected from at least one amino acid substitution, amino acid insertion, amino acid deletion, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14;
- (k)(f) a nucleotide sequence of any of (a) (j)(e) comprising a fragment of at least about 16 nucleotides;
- (1)(g) a nucleotide sequence which hybridizes under at least moderately or highly stringent conditions to the complement of the nucleotide sequence of any of (a), (e), (e), (g), (i) or (k) (f), wherein the encoded polypeptide has an activity of the mature form of a polypeptide as set forth in any of SEQ ID NOs: 2, SEQ ID NO: 4, or SEQ ID NO: 6-or-8; or
- (m) a nucleotide sequence which hybridizes under moderately or highly stringent

conditions to the complement of any of (b), (d), (f), (h), (j) or (k), wherein the polypeptide has an activity of the mature form of a polypeptide as set forth in SEQ ID NOs: 10, 12 or 14; and

(n)(h) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (m)(g).

- 4. (Amended) A vector comprising the nucleic acid molecule of any of Claims 1, 2, or 3.
- The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program-selected from that is GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, andor the Smith-Waterman algorithm.
- 48. (Amended) A viral vector comprising a nucleic acid molecule of <u>any of Claims 1</u>, 2, or 3.
- 55. (Amended) A method of modulating levels of a <u>B7-like</u> polypeptide in an animal comprising administering to the animal the nucleic acid molecule of any of Claims 1, 2, or 3.



EXHIBIT A

	10	20	30 * *		50	60
SEQ01_ORF	ATGGGGCTTG TACCCCGAAC	TGATTTTCCT ACTAAAAGGA	CCACGGTTCT	GGGTCTGGTA CCCAGACCAT	* * ATGAAGTCAT TACTTCAGTA	AGAAGGCCCC TCTTCCGGGG
Marra EST	260 cTGGtcaTcc	270 TGgcTcagCT	280 gacaGcTTCc	GGaTCcaGTt	300 ATcAgaTCAT	310 AGAAGGtCCt>
SEQ01_ORF			1 111	 GGGTCTGGTA	-11 $+$ -11 $+$	
	70 * *	* *	90 * *		110 * *	120
SEQ01_ORF	CAGAATGCAA GTCTTACGTT	CAGTCCTGAA GTCAGGACTT	GGGCTCCCAG CCCGAGGGTC	GCTCGCTTCA CGAGCGAAGT	ACTGCACCGT TGACGTGGCA	CTCCCAGGGC
Marra EST	320 CAGAATGtAA	330 CAGTCCTaAA	340 GGaCTCagAG	GCTCaCTTCA	360 ACTGCACCGT	370 gaCtCAcGGC>
SEQ01_ORF	CAGAATGCAA	CAGTCCTGAA	GGGCTCCCAG	 GCTCGCTTCA	ACTGCACCGT	 CTCCCAGGGC
	130 * *	140 * *	150 * *	160 * *	170 * *	180
SEQ01_ORF	TGGAAGCTCA ACCTTCGAGT	TCATGTGGGC AGTACACCCG	TCTCAGTGAC AGAGTCACTG	ATGGTGGTGC TACCACCACG	TAAGCGTCAG ATTCGCAGTC	GCCCATGGAG CGGGTACCTC
	 380	 390	400	410	a 	120
Marra EST	TGGAAGCTtc	TCATGTGGaC	TCTtAaccAa	ATGGTGGTGC	1 11 11	430 aCCCAaGG-a>
SEQ01_ORF	TGGAAGCTCA	TCATGTGGGC	TCTCAGTGAC	ATGGTGGTGC	TAAGCGTCAG	GCCCATGGAG
SEQ01 ORF	190 * * CCCATCATCA	200 * *	210 * *	220 * * CAGAGGTACG	230	240
2	GGGTAGTAGT	GGTTACTGGC	GAAGTGGAGA	GTCTCCATGC	TGGTCCCGCC	GAACTTCACC CTTGAAGTGG
	440	 450	 460	 	c 480	 490
Marra EST SEQ01 ORF	CCCATCATCA			gccAGtTA-c	1 [1]	cAgCTTCAtC>
	CCCATCATCA				ACCAGGGCGG	GAACTTCACC
SEQ01_ORF	250 * * TCGGAGATGA	260 * * TCATCCACAA	270 * * TGTGGAGCCC .	280 * * AGTGATTCGG (290 * * GGAACATCAG	300 * * ATGCAGCCTC
	AGCCTCTACT 500	AGTAGGTGTT / 510	ACACCTCGGG 520	TCACTAAGCC	CCTTGTAGTC :	FACGTCGGAG
Marra EST	TCGGAGtTGA	TCATCCAtgA	TGTGcAGCCC	1111	1	
SEQ01_ORF	TCGGAGATGA '	rCATCCACAA '	TGTGGAGCCC A	AGTG	1	1

SEQ01_ORF	CUGUACAGI	C GCCTGCATE	G ATCTGCTT	AC CTTACCCTC	C AACTTATCC	360 * * * G AGAGCTGTTC C TCTCGACAAG
SEQ01_ORF	ALICCCAGI	G TTAATCTTG	T AGTCGCTGZ	90 40 * * AG AATGAACCT		20 420 * * C TTGTCTACCC AACAGATGGG
SEQ01_ORF	T CUCUCT GGY	1 CCCGGCTCC	C (-(C-A'l'A'l'T'T'C	60 460 * * * CC TGGGAGCTCG	CTCTCCTCCT	07.00
SEQ01_ORF	AGCIALIALI	TIGITUUGGA	A GCCCAGCGA	0 520 * * * C CTTCAAAGTG G GAAGTTTCAC	CACMCACCAM	CCTCCC
SEQ01_ORF	ACCCCACAGA	GCAATGGGA(: TTTGACTTG	0 580 * * * C GTGGCTACCT G CACCGATGGA	CCTTCTCTCCC	G776666
SEQ01_ORF	AAGICIGCAA	CTGTAAATCT	' CACTGTGAT1	CGGTGTCCCC CGCCACAGGGG	A A C A C A C A C A C A	* * * * * * * * * * * * * * * * * * * *
SEQ01_ORF	AATATICCAG	GIGIATIATC	AAGTTTACCC	700 * * AGTTTAGGTT TCAAATCCAA	TTTTCATTCCC	ma compaga
SEQ01_ORF	AAAGTTGGAC	* * TTGGACTAGC	* * AGGCACCATG	760 * * CTTCTGACGC GAAGACTGCG	* *	
SEQ01_ORF	790 * * CGCTGCTGCT GCGACGACGA	* * GCTGCCGCCG	TCGTTGTTGT	820 * * GGCTGCAACT CCGACGTTGA	CCTCCTCCCC	
SEQ01_ORF	850 * * TGCTGTAGAA ACGACATCTT	GAAAAAGAGG	ATTTCGTATT	* * * CAATTTCAAA A	ለሮአአአሞሮመሮክ ፣	77777777

910 920 930 940 950 960 * * * * * * * * * * * * * SEQ01 ORF ACAAACAAAG AAACTGAGAC AGAAAGTGGA AATGAAAACT CCGGCTACAA TTCAGATGAA TGTTTGTTTC TTTGACTCTG TCTTTCACCT TTACTTTTGA GGCCGATGTT AAGTCTACTT 970 980 990 1000 1010 1020 * * * * * * * * * * * * CAAAAGACCA CAGACACCGC TTCTCTCCCT CCCAAATCCT GTGAATCCAG TGATCCTGAA SEQ01 ORF GTTTTCTGGT GTCTGTGGCG AAGAGAGGGA GGGTTTAGGA CACTTAGGTC ACTAGGACTT 1030 1040 1050 1060 1070 1080 * * * * * * * * * * * * * * * CAAAGAAACA GTAGCTGTGG CCCTCCTCAC CAGCGGGCTG ATCAACGTCC ACCCAGGCCA SEQ01 ORF GTTTCTTTGT CATCGACACC GGGAGGAGTG GTCGCCCGAC TAGTTGCAGG TGGGTCCGGT 1100 1110 1120 1130 1140 * * * * * * * * * * * * 1090 GCAAGTCATC CACAGGCTTC TTTTAATCTG GCCAGTCCTG AGAAGGTCAG TAATACAACT SEQ01 ORF CGTTCAGTAG GTGTCCGAAG AAAATTAGAC CGGTCAGGAC TCTTCCAGTC ATTATGTTGA SEQ01_ORF GTAGTA CATCAT



EXHIBIT B

	- m	י ייניע				
	10 * *					60
SEQ03_ORF	ATGGTGGCAG TACCACCGTC	GAGCCATGGA	AAATAGAGAC	CCACCGGTT	CTGGGTCTGG	TAATGAAGTC ATTACTTCAG
Marra EST	260 aTGcTGat		270 =qc=tch=qC	280	290	300 TtATcAgaTC>
				1 1 11		
SEQ03_ORF	ATGGTGGCAG	GAGCCATGGA	AAATAGAGAC	CCACCCGGTT	CTGGGTCTGG	TAATGAAGTC
	70 * *	80 * *	90 * *	100 * *		
SEQ03_ORF	ATAGAAGGCC TATCTTCCGG 	CCCAAAATGC GGGTTTTACG	AAGAGTCCTG TTCTCAGGAC	AAGGGCTCCC TTCCCGAGGG	AGGCTCGCTT TCCGAGCGAA	CAACTGCACC GTTGACGTGG
Marra EST	310	320	330	340	350	360
maila ESI			AACAGTCCTa	AAGGaCTCag	AGGCTCaCTT	CAACTGCACC>
SEQ03_ORF	ATAGAAGGCC	CCCAAAATGC	AAGAGTCCTG	AAGGGCTCCC	AGGCTCGCTT	CAACTGCACC
	130	140	150 * *	160	170	180
SEQ03_ORF	GTCTCCCAGG CAGAGGGTCC	GCTGGAAGCT CGACCTTCGA	CATCATGTGG	GCTCTCAGTG CGAGAGTCAC	* * ACATGGTGGT TGTACCACCA	* * GCTAAGCGTC CGATTCGCAG
	 	!				l a
	370	380	390	400	410	420
Marra EST	GTgaCtCAcG	GCTGGAAGCT	tcTCATGTGG	aCTCTtAacc	AaATGGTGGT	GCTgAGtcTC>
SEQ03_ORF	GTCTCCCAGG	GCTGGAAGCT	CATCATGTGG	GCTCTCAGTG	ACATGGTGGT	GCTAAGCGTC
	190 * *	200	210	220	230	240
SEQ03_ORF	AGGCCCATGG	AGCCCATCAT	CACCAATGAC	CGCTTCACCT	CTCAGAGGTA	CGACCAGGGC
	TCCGGGTACC	TCGGGTAGTA	GTGGTTACTG	GCGAAGTGGA	GAGTCTCCAT	GCTGGTCCCG
	I 		!			c
Marra EST	430	440	450	460	470	480
narra Est	ccaCCCAaGG	IIIIIIII		CGTTCACCT	aTgccAGtTA	-cAaCAGcat>
SEQ03_ORF	AGGCCCATGG	AGCCCATCAT	CACCAATGAC	CGCTTCACCT	CTCAGAGGTA	CGACCAGGGC
	250	260	270	280	290	300
SEQ03_ORF	* * GGGAACTTCA CCCTTGAAGT	* * CCTCGGAGAT GGAGCCTCTA	* * GATCATCCAC CTAGTAGGTG	* * AATGTGGAGC TTACACCTCG	* * CCAGTGATTC GGTCACTAAG	* * GGGGAACATC CCCCTTGTAG
	490	500 I	510	1	1	!
Marra EST	GacAgCTTCA		GATCATCCAt	520 gATGTGcAGC 		
SEQ03_ORF	GGGAACTTCA	CCTCGGAGAT	GATCATCCAC	AATGTGGAGC	CCAGTG	1

	21.	0 20				
07000	* :	U 32 * *	0 33 * *	0 34 * *	0 35 * *	0 360
SEQU3_ORF	AGATGCAGC	C TCCAGAACA	G TCGCCTGCA	T GGATCTGCT	T ACCTTACCC	T CCAAGTTATG A GGTTCAATAC
	37(*	38	0 39	0 400 * * ;	410	0 420 * * *
SEQ03_ORF	GGAGAGCTGT	TCATTCCCA	G TGTTAATCT	I GTAGTCGCTC	AGAATGAAC	C TTGTGAAGTT G AACACTTCAA
			O TIOLETTI MORE	CATCAGCGAC	, ICTIACTIGO	AACACTTCAA
	430 * *	440	D 45() 46() 47(480
SEQ03_ORF	ACTTGTCTAC	CCTCACACT	GACCTGGCT	CCGGATATT1	CCTGGGAGCT	CCCTCTCCTC
	IGAACAGAIG	GGAGTGTGA	CTGGACCGAC	GGCCTATAAA	GGACCCTCGA	A GCCAGAGGAC
	490 * *	500	510	520	530	540
SEQ03_ORF	GTCAGCCATT	CAAGCTATT <i>E</i>	TTTTGTTCCC	GAGCCCAGCG	ACCTTCAAAG	TCCACTCACC
	CAGTCGGTAA	. GTTCGATAAT	' AAAACAAGGC	CTCGGGTCGC	TGGAAGTTTC	C ACGTCACTCG
	550	560	570	580	590	600 * *
SEQ03_ORF		TGACCCCACA	GAGCAATGGG	ACTTTGACTT	GCGTGGCTAC	CTCCAACACC
	TAGGACCGAG	ACTGGGGTGT	CTCGTTACCC	TGAAACTGAA	CGCACCGATG	GACCTTCTCG
	610	620	630	640	650	660
SEQ03 ORF	* * CTGAAGGCCC	* *	* * AACTCTAAAT	* * * *	* *	660
~ _	GACTTCCGGG	CGTTCAGACG	TTGACATTTA	GAGTGACACT	AAGCCACAGG	CCAAGACACT GGTTCTGTGA
	670	600	600			
CEOO3 ODE	670 * *	* *	690 * *	700 * *	710 * *	720 * *
2FQU2_ORF	GGAGGTGGTA CCTCCACCAT	TTAATATTCC AATTATAAGG	AGGTGTATTA TCCACATAAT	TCAAGTTTAC AGTTCAAATG	CGAGTTTAGG GCTCAAATCC	TTTTTCATTG AAAAAGTAAC
	* *	* *	750 * *	* *	* *	780 * *
SEQ03_ORF	CCTACTTGGG GGATGAACCC	GCAAAGTTGG CGTTTCAACC	ACTTGGACTA TGAACCTGAT	GCAGGCACCA	ТССТТСТСЛС	CCCCACCMCM
				3313331331	ACGARGACIG	CGGCTGCACA
	790 * *	* *	810 * *	820 * *	830	840
SEQ03_ORF	ACTCTTACAA	TACGCTGCTG	CTGCTGCCGC	CGTCGTTGTT	GTGGCTGCAA	* * CTGCTGCTGC
	TGAGAATGTT	ATGUGAUGAU	GACGACGGCG	GCAGCAACAA	CACCGACGTT	GACGACGACG
	850	860	870	880	890	900
SEQ03_ORF	CGTTGTTGTT	* * TCTGCTGTAG	* * AAGAAAAAGA	* * GGATTTCGTA	* * TTCAATTTCA	* *
	GCAACAACAA	AGACGACATC	TTCTTTTTCT	CCTAAAGCAT	AAGTTAAAGT	TTTCTTTAGA

910 920 930 940 950 960 * * * * * * * * * * * * * SEQ03 ORF GAAAAAGAGA AGACAAACAA AGAAACTGAG ACAGAAAGTG GAAATGAAAA CTCCGGCTAC CTTTTCTCT TCTGTTTGTT TCTTTGACTC TGTCTTTCAC CTTTACTTTT GAGGCCGATG 970 980 990 1000 1010 1020 * * * * * * * * * * * * * SEQ03 ORF AATTCAGATG AACAAAAGAC CACAGACACC GCTTCTCTCC CTCCCAAATC CTGTGAATCC TTAAGTCTAC TTGTTTTCTG GTGTCTGTGG CGAAGAGAGG GAGGGTTTAG GACACTTAGG 1030 1040 1050 1060 1070 1080 * * * * * * * * * * * * * * * AGTGATCCTG AACAAAGAAA CAGTAGCTGT GGCCCTCCTC ACCAGCGGGC TGATCAACGT SEQ03_ORF TCACTAGGAC TTGTTTCTTT GTCATCGACA CCGGGAGGAG TGGTCGCCCG ACTAGTTGCA 1090 1100 1110 1120 1130 1140 * * * * * * * * * * * * * * * SEQ03 ORF CCACCCAGGC CAGCAAGTCA TCCACAGGCT TCTTTTAATC TGGCCAGTCC TGAGAAGGTC GGTGGGTCCG GTCGTTCAGT AGGTGTCCGA AGAAAATTAG ACCGGTCAGG ACTCTTCCAG 1150 * * SEQ03_ORF AGTAATACAA CTGTAGTA

TCATTATGTT GACATCAT

3



EXHIBIT C

	10	20	30 * *	4 0 * *	50 * *	60
SEQ05_ORF		ATTTGCTCAC TAAACGAGTG	GGTTCCAGAA	GCTGTAGGTT	CTGGGTCTGG	
Marra EST	250 cTGGctgtGC	260 tggTcaTCct	270 GGc-tCAGct	gacAGcTT	290 CcGGaTCcaG	300 TtATcAgaTC>
SEQ05_ORF		ATTTGCTCAC				
	70	80	90	100	110	120
SEQ05_ORF		CCCAGAATGC GGGTCTTACG	AACAGTCCTG	TTCCCGAGGG		
Marra EST		320 CtCAGAATGt				360 CAACTGCACC>
SEQ05_ORF		CCCAGAATGC				
	130	140	150	160	170	180
SEQ05_ORF		GCTGGAAGCT CGACCTTCGA	CATCATGTGG	GCTCTCAGTG	ACATGGTGGT	GCTAAGCGTC
	370 I	380	300	100	410	a
Marra EST	GTgaCtCAcG		tcTCATGTGG	aCTCTtAacc		420 GCTgAGtcTC>
SEQ05_ORF		GCTGGAAGCT				
	190 * *	200	210	220	230	240
SEQ05_ORF		AGCCCATCAT TCGGGTAGTA				
	430	 	450	 460	 	c 480
Marra EST			CACCAAcaAC	CGtTTCACCT		-cAaCAGcat>
SEQ05_ORF	AGGCCCATGG	AGCCCATCAT	CACCAATGAC	CGCTTCACCT	CTCAGAGGTA	CGACCAGGGC
	250 * *	260	270	280	290	300 * *
SEQ05_ORF		CCTCGGAGAT GGAGCCTCTA	GATCATCCAC	AATGTGGAGC	CCAGTGATTC	GGGGAACATC
Marra EST		500 tCTCGGAGtT				
SEQ05_ORF						

	310 * *	320	330	340	350	360 * *
SEQ05_ORF	AGATGCAGCC	TCCAGAACAG	TCGCCTGCAT	GGATCTGCTT	ACCTTACCGT	CCAAGTTATG GGTTCAATAC
SEOUS ODE	370 * *	380 * *	390 * *	400 * *	410	420
SEQUO_ORF	GGAGAGCTGT CCTCTCGACA	AGTAAGGGTC	ACAATTAGAA	CATCAGCGAC	TCTTACTTGG	AACACTTCAA
	430 * *	440 * *	450 * *	460 * *	470 * *	480 * *
SEQ05_ORF	ACTTGTCTAC	CCTCACACTG	GACCCGGCTC	CCGGATATTT	CCTGGGAGCT	
	490 * *	500 * *	510 * *	520 * *	530 * *	540 * *
SEQ05_ORF	GTCAGCCATT CAGTCGGTAA					TGCAGTGAGC ACGTCACTCG
	550 * *	560 * *	570 * *	580 * *	590 * *	600 * *
SEQ05_ORF	ATCCTGGCTC	TGACCCCACA	GAGCAATGGG	ACTTTGACTT		CTGGAAGAGC
	610 * *	620 * *	630 * *	640	650 * *	660
SEQ05_ORF	CTGAAGGCCC	GCAAGTCTGC	AACTGTAAAT	CTCACTGTGA		CCAAGACACT
	670 * *	680 * *	690	700	710 * *	720
SEQ05_ORF	GGAGGTGGTA	TTAATATTCC	AGGTGTATTA	TCAAGTTTAC	CGAGTTTAGG GCTCAAATCC	TTTTTCATTG
	730	740	750	760	770 * *	780
SEQ05_ORF	CCTACTTGGG	GCAAAGTTGG	ACTTGGACTA	GCAGGCACCA	TGCTTCTGAC ACGAAGACTG	GCCGACGTGT
	790 * *	800	810	820	830 * *	840
SEQ05_ORF	ACTCTTACAA	TACGCTGCTG	CTGCTGCCGC	CGTCGTTGTT		CTGCTGCTGC
	850 * *	860	870	880	890 * *	900
SEQ05_ORF	CGTTGTTGTT	TCTGCTGTAG	AAGAAAAAGA	GGATTTCGTA		AAAGAAATCT

	910	920	930	940	950	960
SEQ05_ORF			AGAAACTGAG	ACAGAAAGTG	GAAATGAAAA	
SEQ05_ORF		980 * * AACAAAAGAC TTGTTTTCTG	* * CACAGAAACC			
SEQ05_ORF		1040 * * AACAAAGAAA TTGTTTCTTT	* * CAGTAGCTGT			
SEQ05_ORF		1100 * * CAGCAAGTCA GTCGTTCAGT				* * TGAGAAGGTC
SEQ05_ORF	1150 * * AGTAATACAA TCATTATGTT					